REMARKS

Claims 18-27 are submitted hereby in place of claims 13-17.

The specification is amended, hereby, in connection with the definition of variables R_1-R_4, found in the sequence formulas at page 3, in order to reinstate the definitions as described in the application as originally filed (the previously submitted Amendment contained an amended definition). The requisite marked up version is attached, hereto.

Claims 18-27 contain subject matter of claims 6-12. More precisely, claim 18 corresponds to claim 7, except that the "fragment" is no longer recited in the claim (also, sequence identifiers are inserted for each of the recited sequences). Claim 19 corresponds to claim 8 written as in independent claim. Method claim 20 corresponds to claim 9 revised to address issues raised in the §112, paragraph 2, rejection of record, as explained further, below. Method claim 21 corresponds to method claim 10 and incorporates subject matter of claim 7. Claims 22 and 23 define the peptide made by the method of claims 20 and 21, respectively. Claim 24 corresponds to claim 12, revised to recite that the "peptide" is administered in "an effective amount." Claims 25, 26, and 27 correspond to claim 24, made dependent on claims 19, 22, and 23, respectively.

Claims 28 and 29 define a composition of the invention, containing the peptide of claims 18 and 19, respectively, in combination with a physiologically acceptable excipient in a galenic formulation, as described in the specification at page 4, paragraph 4.

Sequence identifiers are inserted adjacent corresponding sequences at page 3 of the specification, which overcomes the corresponding objection in the Office Action. The objection to

the specification in connection with the definition of variables R_1 and R_4 cannot be sustained for the same reasons provided, below, in connection with the rejection under §112, paragraph 2.

The objection to claim 7 is overcome by inserting corresponding sequence identifiers for each sequence recited in the claim, i.e., present claim 18. As for use of the single letter code for the amino acids sequences in the claims, attention is directed, again, to 37 CFR 1.821(a)(2).

Claims 6-12 were rejected under 35 USC 112, first paragraph, for allegedly lacking enablement. Reconsideration is requested.

According to the statement of rejection, the specification lacks enablement except for peptides specifically described in the specification, i.e., those sequences found in the Sequence Listing.

First of all, claim 8 defines the "peptide" in terms of only sequences specifically described in the instant application, i.e., sequences described at specification page 3, which represent SEQ ID NO.: 8, 14, and 15. Accordingly, in view of the criteria set forth in the statutory rejection, the rejection as applied against claim 8 is in order of withdrawal (and, the rejection cannot be applied against present, corresponding claim 19).

With regard to the alleged failure to satisfy the requirements §112, ¶1, in connection with the "N-modified" peptide, one skilled in the art would have possessed the knowledge needed, in conjunction with the teachings of the instant application, to readily effect the "N-modified" peptide by "amidation, acetylation, sulfation, phosphorylation, glycosylation, or oxidation," such that the

"bifidogenic properties" of the non-modified peptide are retained. Such knowledge is exemplified by:

- *Peptide Synthesis Protocols.* Edited by M. W. Pennington and B.M. Dunn, Humana Press, 1994.
- *the Chemical Synthesis of Peptides.* J. Jones, Clarendon Press, 1991.

Although published at a later date, the general knowledge of the skilled artisan at the time of invention is reflected by:

- *Fmoc Solid Phase Peptide Synthesis. A Practical Approach.* Edited by W.C. Chan and P.D. White, Oxford University Press, 2000
- Synthese von Peptiden. Editor-in-chief: M. Goodman; Houben-Weyl, *Organic Chemistry, Vol. E22a*, Methods in Synthesis of Peptides and Pepti-domimetics. Thieme, 2001.

In connection with the alleged lack of satisfying §112, ¶1, regarding synthesis of phosphopeptides, glycopeptide synthesis, and peptide sulfate synthesis, attention is directed to:

- Synthesis of phosphopeptides:

  Methods in Enzymology, 289, 245-66 (1997), "Synthesis of phosphopeptides using modern chemical approaches." J. W. Perich.
- Glycopeptide synthesis:

  Current Protein and Peptide Science, 1, 23-48 (2000), "Recent progress in the solid-phase synthesis of glycopeptide." H. Jojo and Y. Nakahara..

- Peptide sulfate synthesis:

  Yakugaku Zasshi, 118, 493-510 (1998), "Peptide synthesis aiming at elucidation and creation of protein functions" (Article in Japanese). S. Futaki.

As demonstrated by the foregoing cited documents, the knowledge necessary make the N-modified peptide of the invention, i.e., by amidation, acetylation, sulfation, phosphorylation, glycosylation, or oxidation, is possessed by one of ordinary skill in the art, and, therefore, need not be described in detail in the specification. "Non-critical features of the invention may be supported by a more general disclosure than those at the heart of the invention." *In re Stephens*, 188 USPQ 659, 661 (CCPA 1976).

With respect to determining which protein variants (i.e., N-modified proteins) have bifidogenic activity, this does not involve undue experimentation, allegations to the contrary and the statement of rejection notwithstanding. Screening a protein "variant" for biological activity is routine, not undue, experimentation. *Ex parte Mark*, 12 USPQ2d 1904 (Bd. Pat. App. & Inter. 1989).

The statement of rejection refers to description in the specification (pages 4-5) in connection with the treatment of various diseases in accordance with the instant invention. It must be remembered that §112, paragraph 1, does not require enablement of all uses of the invention that are described in the application. Only one use in specification need be enabled in order to satisfy the requirements of §112, ¶1. Total incapacity, i.e., incapacity with respect to *all* uses of the invention described in the specification, is necessary to demonstrate lack of enablement with respect to the

invention claimed. *Tol-O-Matic Inc. v. Proma Produkt-Und Marketing Gesellschaft m.b.H.*, 20 USPQ2d 1332, 1338 (Fed. Cir. 1991). When the claims "do not require" the subject matter at issue, enablement with respect to such subject matter is not required under § 112, paragraph one. *Ex parte Erlich*, 3 USPQ2d 1011, 1014 (BPA&I 1987). "An invention need not be the best way or the only way to accomplish a certain result, and *it need only be useful to some extent* and in certain applications." *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1094, 1100 (Fed. Cir. 1991).

According to the statement of rejection (Office Action, page 7, second complete paragraph), enablement is lacking because, allegedly, "the treating conditions such as the dose for various compounds [of the invention] are not described in the specification." The statement of rejection is incorrect in this respect. Contrary to the aforesaid allegation, treatment dosage is, in fact, described at page 4, paragraph 5, of the specification.

According to the statement of rejection (page 7, penultimate paragraph), there is lack of enablement because the claims include embodiments (i.e., N-modified variants), which are not specifically disclosed. The statement of rejection is mistaken in this respect. Lack of enablement under §112 is not established by mere allegations of undue breadth, that is, by merely arguing that claims read on non-disclosed embodiments. *Horton v. Stevens*, 7 USPQ2d 1245 (BPA & I 1988). In order to satisfy the requirements of §112, first paragraph, "it is not necessary to embrace in the claims or describe in the specification all possible forms in which the claimed principle may be reduced to practice." *Smith v. Snow*, 294 U.S. 1, 11 (1935). The law does not require an applicant to describe in his specification every conceivable embodiment of the invention. *SRI Int'l v.*

Matsushita Elec. Corp. of America, 227 USPQ 577, 586 (Fed. Cir. 1985). Moreover, while working examples drawn to specific embodiments may be desirable, they are not *required* in order to satisfy enablement under §112. *In re Strahilevitz*, 212 USPQ 561 (CCPA 1982). It is well established that working examples are not necessary when one possessed of knowledge of ordinary skill in the art could practice the invention without the exercise of undue experimentation. *Ex parte Nardi*, 229 USPQ 79 (BPA & I 1986). As explained, above, one skilled in the art possesses the knowledge necessary to practice the presently claimed invention (i.e., in view of the teachings of the invention provided in the present application). "In satisfying the enablement requirement, an application need not teach, and preferably omits, that which is well known in the art." *Staehelin v. Secher*, 24 USPQ2d 1513, 1516 (BPA & I 1992).

Claims 5-12 were rejected under 35 USC 112, paragraph 1, for allegedly failing to satisfy the written description requirement, i.e., it is alleged that the application as filed would not have reasonably conveyed to one skilled in the art that Applicants had possession of the invention as claimed. Reconsideration of the rejection is requested.

First of all, attention is directed to the fact that the peptide "fragments" subject matter is not found in the present claims. Accordingly, to the extent that the rejection concerns this subject matter, the rejection is rendered moot.

Accordingly the statement of rejection (Office Action, page 9), the written description requirement of §112, paragraph 1, is not satisfied because, of the alleged "lack of a structure to

function/activity relationship and the lack of representative species for the derivatives . . . of the peptides having by bifidogenic properties." The statement of rejection is incorrect in this respect.

First, the alleged failure to describe "structure" as it relates to the function of the invention does not support the rejection. The first paragraph of § 112 contains no requirement for a *structural* disclosure - a description entirely in *functional* terms can satisfy the enablement requirement. *Ex parte Butler*, 217 USPQ 290 (USPTO Bd. App. 1982). *See*, also, *In re Donohue*, 193 USPQ 136 (CCPA 1977), *Ex parte Billottet*, 192 USPQ 414 (USPTO Bd. App. 1976). Particularly when details of the *structure* at issue are not a critical aspect of the invention claimed, a detailed description of what would be readily apparent to one of ordinary skill in the art serves no practical purpose. "Non-critical features of the invention may be supported by a more general disclosure than those at the heart of the invention." *Stephens*, 188 USPQ at 661. In the present case, "amidation, acetylation, sulfation, phosphorylation, glycosylation, or oxidation" of the recited (peptide) sequences would effect a peptide structural modification readily apparent to one of ordinary skill in the art. As such, there is no need to provide a detailed description of the structural modification.

Also, the fact that the claims cover non-disclosed embodiments does not support the rejection. Under the written description requirement of §112, ¶1, the concern of the PTO is support or non-support for a generic term, not its breadth. *In re Marcozzi*, 169 USPQ 367, 369 (CCPA 1971).

Claims 6-8 and 10-12 were rejected under 35 USC 112, second paragraph, as allegedly being indefinite. Reconsideration is requested.

First of all, to the extent the rejection concerns the "fragment" subject matter of the invention, the rejection is rendered moot, since the present claims do not contain the "fragment" subject matter. Secondly, the claims are amended, hereby, to address some of the alleged instances of indefinite claim language, and the allegations with respect to the remaining alleged instances of indefinite claim language are poorly taken, as explained below. Also, the rejection is rendered moot to the extension it applies to "combination peptides" subject matter of the invention, as this subject matter is not contained in the present claims.

The §112, ¶2, rejection alleges: "Claim 12 is indefinite because it lacks essential steps . . . [and] the omitted step is the effective amount of the peptide used and the outcome of the treatment" (Office Action, page 10). The rejection is inapplicable against present corresponding claims 24-27.

Each of present claims 24-27 recites "an effective amount" of the protein is administered. The amount need not be quantified, and the treatment outcome need not be recited, to satisfy §112, ¶2. Reciting "an effective amount" of the treatment composition is sufficient to satisfy the requirements §112, ¶2, and the function to be achieved by the treatment need not be recited in the claim. *Ex parte Skuballa*, 12 USPQ2d 1570 (Bd. Pat. App. & Inter. 1989). There is nothing indefinite about defining amounts using functional criteria. *In re Spiller*, 182 USPQ 614 (CCPA).

As to the allegation of indefiniteness because of omitted steps, it must be remembered that "it is not necessary that a claim recite each and every element needed for the practical utilization of the claimed subject matter." *Carl Zeiss Stiftung*, 20 USPQ2d at 1101. The details of *how* the invention is to be *practiced* is the function of the specification, not the claims, the function of which

is to define the legal limits of the invention. *In re Roberts*, 176 USPQ 313, 315 (CCPA 1973). As indicated, above, the dosage amounts necessary for how to practice the invention are described in the present specification (i.e., at page 4, ¶5).

According to the statement of rejection, the term "N-modified," is allegedly indefinite because it is generic, i.e., it broadly encompasses two non-recited alternatives. This reflects concern about the scope of the language at issue. As such, the inquiry has no bearing on whether the term is indefinite under §112, ¶2, since claim "breadth is not to be equated with indefiniteness." *In re Miller*, 169 USPQ 597, 600 (CCPA 1970). Even when an "undoubtedly large number" of embodiments fall within the scope of a generic expression "the expression is not for that reason indefinite." *In re Skoll*, 187 USPQ 481, 482 (CCPA 1975).

In connection with the definitions of variables R_1-R_4 in claim 7 (i.e., present claim 18), the definitions are not indefinite. It is applicant's sole prerogative to define the claims. *In re Pilkington*, 162 USPQ 145, 148 (CCPA 1969). The Examiner's definition of a claim limitation cannot conflict with the definition given in the specification. *In re Zletz*, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989). The examiner must use the specification definition in construing the claims for comparison with the prior art.

> When the applicant states the meaning that the claim terms are intended to have, the claims are examined with that meaning, in order to achieve a complete exploration of the applicant's invention and its relation to the prior art.

Zletz, 13 USPQ2d at 1322. Claim terms need not be "conventional" in the art, since a patent applicant is entitled to be his own lexicographer. *In re Castaing*, 166 USPQ 550 (CCPA 1970).

Also, while *limitations* from the specification cannot be read into the claims, words in the specification are properly used during prosecution as an aid in *interpret existing claim limitations*. The PTO has been cautioned not to confuse the former with the later.

> The Commissioner confuses [1] impermissibly imputing limitations from the specification with [2] properly referring to the specification to determine the meaning of a particular word or phrase recited in a claim.

In re Donaldson Co. Inc., 29 USPQ2d 1845, 1850 (Fed. Cir. 1994). Merely that it requires some thought to understand the meaning of a claim term does not render the term indefinite under §112, ¶2.

> The purpose of the claims is not to explain the technology or how it works, but to state the legal boundaries of the patent grant. A claim is not "indefinite" simply because it is hard to understand when viewed without benefit of the specification.

S3 Inc. v. nVIDIA Corp., 59 USPQ2d 1745, 1748 (Fed. Cir. 2001).

Moreover, representations of amino acid sequences with "NH_2" and "COOH" at the amino and carboxyl ends, respectively, e.g., NH_2-G-D-F-R-G-COOH, is a well known convention in the art at the time of invention, as illustrated by Stryer, *BIOCHEMISTRY*, W. H. Freeman and Company, 1981 (ISBN 0-7167-1226-1), pages 23 and 24 (copies attached, hereto). As such, the definitions of variables R_1-R_8 in claim 7 (and in present claim 18) are not indefinite. While claims are to be given their broadest reasonable interpretation during prosecution, the definition of a claim limitation given by the Examiner cannot be different than would be given by one of ordinary skill in the art. *In re Cortright*, 49 USPQ2d 1464 (Fed. Cir. 1999). The correct test for indefinite claim language is

whether one of ordinary skill in the art would be confused as to the meaning of subject matter defined by the language at issue. *In re Kroekel*, 183 USPQ 610 (CCPA 1974).

Accordingly, the rejection as applied against claim 7 is in order to be withdrawn, and the rejection cannot be applied against present claim 18.

Favorable action is requested.

Respectfully submitted,

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Attachments - Marked up version of amendments to the specification
- Stryer, *BIOCHEMISTRY*, W. H. Freeman and Company, 1981 (ISBN 0-7167-1226-1), pages 23 and 24

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Marked up version of amendments to the specification

IN THE SPECIFICATION

Rewrite page 3 (twice amended), line 6-last line, as:

Preferably, peptides are used which have the following amino acid sequences:

R_1-EQLLRLKK-R_2 (SEQ ID NO: 1), R_1-YLEQLLRLKKY-R_2 (SEQ ID NO: 2),

R_1-NFQRNILR-R_2 (SEQ ID NO: 3), R_1-YMNGMNRQRNILR-R (SEQ ID NO: 4),

R_1-FQWQRNMRK-R_2 (SEQ ID NO: 5), R_1-HTGLRRTA-R_2 (SEQ ID NO: 6),

R_1-FTAIQNLRK-R_2 (SEQ ID NO: 7), R_1-EVAARARVVW-R_2 (SEQ ID NO: 8),

R_1-WQRNMRKV-R_2 (SEQ ID NO: 9), R_1-LARTLKRLK-R_2 (SEQ ID NO: 10),

R_1-YFQKVEKV-R_2 (SEQ ID NO: 11), R_1-LVRYTKKV-R_2 (SEQ ID NO: 12),

R_1-KYLYEIARR-R_2 (SEQ ID NO: 13), R_1-ARRARVVWCAVG-R_2 (SEQ ID NO: 14),
R_3-CIAL-R_4 (SEQ ID NO: 15)

R_1-AFRARVVWCAVGE-R_2 (SEQ ID NO: 16),
R_3-CIAL-R_4 (SEQ ID NO: 15)

R_1-YQRRPAIAINNPYVPRTYYANPAVVRPHAQIPQRQYLPNSHPPTVVRRPNLHPSF-R_2,
(SEQ ID NO: 17)

R_1-GHRRRSVQWCTVSQPEATKCFQWQRNMRKVRGPPVSCIKRDSPIQCIQA-R_2
(SEQ ID NO: 18),

R_1-GHRRSVQWCAVSQPEATKCFQWQRNMRKVRGPPVSCIKRDSPIQCIQA-R_2,
(SEQ ID NO: 19),

R_1-GHRRRSVQWCAVSQPEATKCFQWQRNMRKVRGPPVSCIKRDSPIQ CIQA-R,
(SEQ ID NO: 20),

R_1-VHQHQKAMPKPWIQPKTKVIPYVRYL-R_2 (SEQ ID NO: 21),

R_1-AFRARVVWAAVG-R_2 (SEQ ID NO: 22),

R_1-CAVGGGCIAL-R_2 (SEQ ID NO: 23),

R_1-RHTRKYWCRQGARGGCITL-R_2 (SEQ ID NO: 24),

wherein

[R_1, R_2, R_3, and R_4 are optionally present,]

R_1, R_3 independently represents NH_2, an amino acid, or a peptide containing up to 100 amino acids, and

R_2, R_4 independently represents COOH, $CONH_2$, an amino acid, or a peptide containing up to 100 amino acids;

and the amided acetylated, sulfated, phosphorylated, glycosylated, oxidixed derivatives or fragments thereof having bifidogenic properties.

Second Edition

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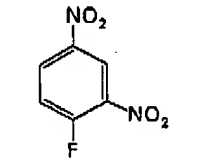
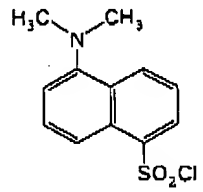
covalent link (Figure 2-27). *Fluorodinitrobenzene* (FDNB), first used for this purpose by Sanger, reacts with the uncharged α-NH_2 group to form a yellow dinitrophenyl (DNP) derivative of the peptide. The bond between the DNP and the terminal amino group is stable under conditions that hydrolyze peptide bonds. Hydrolysis of the DNP-peptide in 6 N HCl yields a DNP-amino acid, which is identified as DNP-alanine by its chromatographic properties.



Fluorodinitrobenzene

Dansyl chloride is now often used to identify amino-terminal residues. It reacts with amino groups to form highly fluorescent and stable sulfonamide derivatives. A few nanograms of an amino-terminal residue can be identified after acid hydrolysis of peptide bonds.



Dansyl chloride

Although the DNP and dansyl methods for the determination of the amino-terminal residue are powerful, they cannot be used repetitively on the same peptide because the peptide is totally de-

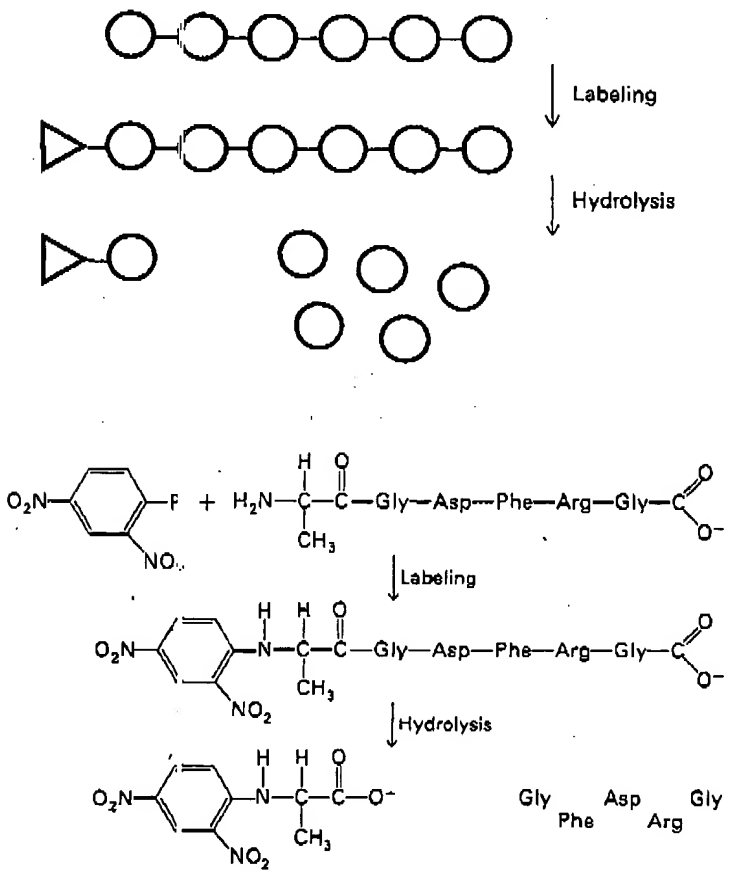


Figure 2-27
Determination of the amino-terminal residue of a peptide. Fluorodinitrobenzene (Sanger's reagent) is used to label the peptide, which is then hydrolyzed. The DNP-amino acid (DNP-alanine in this example) is identified by its chromatographic characteristics.

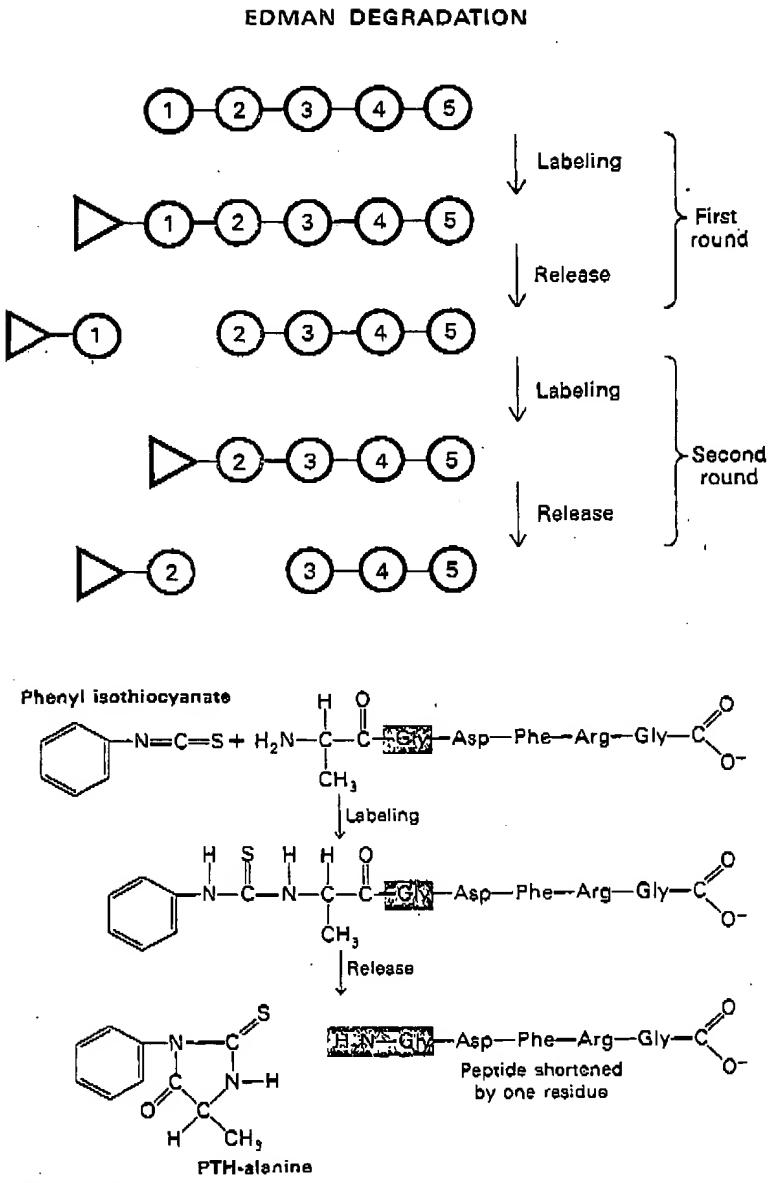


Figure 2-28
The Edman degradation. The labeled amino-terminal residue (PTH-alanine in the first round) can be released without hydrolyzing the rest of the peptide. Hence, the amino-terminal residue of the shortened peptide (Gly-Asp-Phe-Arg-Gly) can be determined in the second round. Three more rounds of the Edman degradation reveal the complete sequence of the original peptide.